



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Hubei province, who would be strictly followed up through home visits and by telephone by community management staff.

Mathematical models have been used to simulate scenarios and predict evolution of infectious diseases since the early 20th century.¹¹ Models are usually driven by a disease's intrinsic mechanism or fitted through sufficient data, but they are frequently expected to provide quick insights of, and predictive power on, a new pathogen in the early stages of an outbreak, which are seemingly contradictory expectations.^{2,12} Indeed, it is not clear whether early cases of COVID-19 were from infection by animal or human, and data are limited and unreliable. In this case, models fitted by early data probably produce results divorced from reality. Early modelling studies have proved overly optimistic about the situation in Wuhan.¹² The closer to reality, the more resources a model requires. Modellers must compromise with reality most of the time.

As data are shared, and computing performance improves (including artificial intelligence), we believe that the above contradictions will be alleviated. Mathematical modelling will have a greater role in supporting clinical diagnosis and optimising a combination of strategies. In view of substantial data accumulated for COVID-19, an essential next step is to estimate whether a second wave of COVID-19 will appear in China.

ZJ declares grants from the National Natural Science Foundation of China (91546203, 91846302). ZL declares grants from the Ministry of Science and Technology of the People's Republic of China.

*Zhongwei Jia, Zuhong Lu
urchinjj@163.com

National Institute on Drug Dependence, School of Public Health, Peking University, Beijing 100191, China (ZJ); Center for Drug Abuse Control and Prevention, National Institute of Health Data Science, Peking University, Beijing, China (ZJ); and State Key Laboratory for Bioelectronics, School of Biological Science and Medical Engineering, Southeast University, Nanjing, China (ZL)

- 1 John Hopkins Bloomberg School of Public Health. 2019 Global Health Security Index: building collective action and accountability. October, 2019. <https://www.ghsindex.org/wp-content/uploads/2019/10/2019-Global-Health-Security-Index.pdf> (accessed March 17, 2020).
- 2 Niehus R, De Salazar AM, Taylor AR, Lipsitch M. Using observational data to quantify bias of traveller-derived COVID-19 prevalence estimates in Wuhan, China. *Lancet Infect Dis* 2020; published online April 1. [https://doi.org/10.1016/S1473-3099\(20\)30229-2](https://doi.org/10.1016/S1473-3099(20)30229-2).
- 3 Day M. Covid-19: surge in cases in Italy and South Korea makes pandemic look more likely. *BMJ* 2020; **368**: m751.
- 4 Jernigan DB, CDC COVID-19 Response Team. Update: public health response to the coronavirus disease 2019 outbreak — United States, February 24, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69**: 216–19.
- 5 Tang XL, Wu CC, Li X, et al. On the origin and continuing evolution of SARS-CoV-2. *Nat Sci Rev* 2020; published online March 3. DOI:10.1093/nsr/nwaa036.
- 6 Cohen J. Wuhan seafood market may not be source of novel virus spreading globally. *Science* 2020; published online Jan 26. <https://www.sciencemag.org/news/2020/01/wuhan-seafood-market-may-not-be-source-novel-virus-spreading-globally> (accessed March 24, 2020).
- 7 Matsuda T, Suzuki H, Ogata N. Phylogenetic analyses of the severe acute respiratory syndrome coronavirus 2 reflected the several routes of introduction to Taiwan, the United States, and Japan. Feb 28, 2020. <https://arxiv.org/abs/2002.08802> (accessed March 24, 2020).
- 8 Battegay M, Kuehl R, Tschudin-Sutter S, Hirsch HH, Widmer AF, Neher RA. 2019-novel coronavirus (2019-nCoV): estimating the case fatality rate—a word of caution. *Swiss Med Wkly* 2020; **150**: w20203.
- 9 Chinadaily. Just the facts on mobile cabin hospitals. Feb 5, 2020. http://www.chinadaily.com.cn/a/202002/05/WS5e3a8309a3101282172752f5_1.html (accessed March 24, 2020).
- 10 National Health Commission of the People's Republic of China. Update on the data of COVID-19 outbreak as at 24:00 on 19 March. March 20, 2020. <http://www.nhc.gov.cn/xcs/yqtb/202003/0fc43d6804b04a4595a2eadd846c0a6e.shtml> (accessed March 20, 2020).
- 11 Hamer WH. The Milroy Lectures on epidemic disease in England: the evidence of variability and persistency of type. *Lancet* 1906; **167**: 655–62.
- 12 Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; published online Jan 29. DOI:10.1056/NEJMoa2001316.



The important role of serology for COVID-19 control

Published Online

April 21, 2020

[https://doi.org/10.1016/S1473-3099\(20\)30322-4](https://doi.org/10.1016/S1473-3099(20)30322-4)

See [Articles](#) page 809

As of April 14, 2020, just under 2 million cases of coronavirus disease 2019 (COVID-19) have been reported worldwide.¹ With the pandemic growing at an alarming rate and national governments struggling to control local epidemics because of scant diagnostics and impermanent non-pharmaceutical interventions, we should look to additional epidemiological solutions. Locations such as Singapore and Taiwan have been successful in slowing epidemic growth by using intensive surveillance with broader testing strategies to identify and contain cases.^{2,3}

In *The Lancet Infectious Diseases*, Sarah Ee Fang Yong and colleagues⁴ report three clusters of COVID-19 cases identified in Singapore in early 2020 by active case-finding and contact tracing and confirmed with RT-PCR. One cluster from a church (Church A) was previously identified⁵ and linked to two imported cases from Wuhan, China. The two additional clusters (Church B and a family gathering) were attributable to community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by one individual interacting with both clusters. Serological platforms were

developed and assessed for confirmation of SARS-CoV-2-specific antibody responses to capture past infections. By serological analysis, Yong and colleagues identified the missing link between the Church A cluster and the other two clusters—an individual who had twice tested negative by RT-PCR. By linking all three clusters, Yong and colleagues highlight the success of such surveillance measures to capture many cases and effectively slow the spread of COVID-19 in Singapore.

This investigation exemplifies the failings of RT-PCR as a sole diagnostic method in surveillance, because of its inability to detect past infection, and the added value of serological testing, which if captured within the correct timeframe after disease onset can detect both active and past infections.^{6,7} In public health practice, serological analysis can be useful for rapid case-identification and the subsequent chain of events to actively identify close contacts, recommend quarantine, and define clusters of cases. Contact tracing, which is a necessary but insufficient means of disease control, needs careful effort and is sensitive to timing to be effective, particularly in highly dense populations. As shown in Singapore, serological analysis can be useful for contact tracing in urban environments and linking clusters of cases retrospectively to delineate transmission chains and ascertain how long transmission has been ongoing or to estimate the proportion of asymptomatic individuals in the population.

Beyond the immediate use of serological data to identify and contain cases, these data can also be used to set control policies. Population serological testing (specifically measuring SARS-CoV-2-specific IgG antibody titres) can estimate the total number of infections by assessing the number of individuals who have mounted an immune response, regardless of whether an infection was subclinical or happened in the recent past (current data suggest antibodies persist for at least 4 weeks).⁸ By providing estimates of who is and is not immune to SARS-CoV-2, serological data can be used in at least four ways. First, to estimate epidemiological variables, such as the attack rate or case-fatality rate, which are necessary to assess how much community transmission has occurred and its burden. Second, to strategically deploy immune health-care workers to reduce exposure of the virus to susceptible individuals. Third, to assess the effect of non-pharmaceutical interventions at the population-level and inform policy changes to release such measures. Fourth, to identify

individuals who mounted a strong immunological response to the virus and whose antibody isolates can be used to treat patients via plasma therapy.⁹

Although the potential for serological assays to help control the COVID-19 pandemic is substantial, the complexity of developing and validating a diagnostic test is not fully elucidated by Yong and colleagues.⁴ Serological assays are currently being developed for widespread use.¹⁰ Yet, several challenges remain: first, assessing the sensitivity and specificity of tests, particularly for determining disease during the acute phase of infection; second, verifying the test is not detecting cross-reactivity with other viral pathogens that result in false-positive results; third, understanding antibody kinetics over time to distinguish thresholds of immunity, because we do not know how long immunity to this novel coronavirus might last; and finally, ensuring the test is reliable for distribution and is cost-efficient. Although RT-PCR diagnostics will still be vital for identifying acute infection, as the SARS-CoV-2 pandemic continues to spread and cases accumulate, serological testing and data will prove increasingly important to understand the pandemics' past and predict its future.

We declare no competing interests.

*Amy K Winter, Sonia T Hegde
akwinter@jhu.edu

Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA

- 1 Dong E, Du H, Gardner L. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). April 14, 2020. <https://coronavirus.jhu.edu/map.html> (accessed April 9, 2020).
- 2 Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing. *JAMA* 2020; published online March 3. DOI:10.1001/jama.2020.3151.
- 3 Lee VJ, Chiew CJ, Khong WX. Interrupting transmission of COVID-19: lessons from containment efforts in Singapore. *J Travel Med* 2020; published online March 13. DOI:10.1093/jtm/taaa039.
- 4 Yong SEF, Anderson DE, Wei WE, et al. Connecting clusters of COVID-19: an epidemiological and serological investigation. *Lancet Infect Dis* 2020; published online April 21. [https://doi.org/10.1016/S1473-3099\(20\)30273-5](https://doi.org/10.1016/S1473-3099(20)30273-5).
- 5 Pung R, Chiew CJ, Young BE, et al. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. *Lancet* 2020; **395**: 1039–46.
- 6 Lou B, Li T-D, Zheng S-F, et al. Serology characteristics of SARS-CoV-2 infection since the exposure and post symptoms onset. *medRxiv* 2020; published online March 27. DOI:10.1101/2020.03.23.20041707 (preprint).
- 7 Haveri A, Smura T, Kuivanen S, et al. Serological and molecular findings during SARS-CoV-2 infection: the first case study in Finland, January to February 2020. *Euro Surveill* 2020; **25**: 2000266.
- 8 Bao L, Deng W, Gao H, et al. Reinfection could not occur in SARS-CoV-2 infected rhesus macaques. *bioRxiv* 2020; published online March 14. DOI:10.1101/2020.03.13.990226 (preprint).
- 9 Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis* 2020; **20**: 398–400.
- 10 Amanat F, Nguyen T, Chromikova V, et al. A serological assay to detect SARS-CoV-2 seroconversion in humans. *medRxiv* 2020; published online March 18. DOI:10.1101/2020.03.17.20037713.



Flickr - Roberto Herdianto